REMARKS

Status of the Claims

Claims 1-20 are currently pending in the present application. Claims 1, 7, 8 and 16 are amended. Claim 6 is cancelled. No new matter is added. In light of the remarks herein, reconsideration of claims 1-5 and 7-20 is respectfully requested.

Amendments to the Claims

Claims 1, 7, 8 and 16 are amended. Claims 1 and 16 are amended to recite "in a subject *with age associated DNA* damage." Claim 1 is further amended to recite "about 0.1 to 20 mg lutein, beta-carotene and lycopene, *wherein the beta-carotene and lycopene are present* in amounts sufficient to act synergistically with lutein to *decrease age associated DNA damage in the subject*." Claim 16 is further amended to recite "about 0.1 to 20 mg lutein, and *sufficient amounts of* beta-carotene and lycopene *to act synergistically with lutein*, whereby *age associated* DNA damage in the subject." Support for the amendments to claims 1 and 16 can be found throughout the application as filed and, for example, in paragraphs [0005] and [0087]-[0088] of the published application. Claim 8 is amended to recite "a method of decreasing *oxidative DNA damage* in a subject *with a free-radical associated disorder* comprising: administering a synergistic combination of carotenoids to the subject, wherein the synergistic combination comprises about 0.1 to 20 mg lutein, and *sufficient amounts of beta-carotene and lycopene to act synergistically with lutein to decrease oxidative DNA damage in the subject*." Support for the amendments to claim 8 can be found throughout the application as filed and, for example, in paragraphs [0010], [0023] and [0087]-[0088] of the published application. Claims 7 is amended to correct dependency in light of the cancellation of claim 6. No new matter is added.

The Claimed Invention

The present invention is directed to pharmaceutical compositions and methods for decreasing DNA damage in a subject by administering a synergistic combination of carotenoids comprising about 0.1 to 20 mg lutein, beta-carotene and lycopene, wherein the beta-carotene and lycopene are present in amounts sufficient to act synergistically with lutein to decrease age associated or oxidative DNA damage in the subject.

Novelty of the Pending Claims

Claims 1-3, 5-10, 13 and 15-18 stand rejected under 35 U.S.C. 102(b) as being anticipated by Babish et al. (US Pub. No. 2002/0110604 A1) as evidenced by Hoshino et al. (US Patent No. 6,869,773). The Office Action cites Babish as teaching a carotenoid species. The Office Action concedes that Babish does not teach the carotenoid species for treating aging. The Office Action further cites Hoshino to demonstrate that aging is inherently caused by oxidative damage. However, Babish as evidenced by Hoshino does not teach or suggest a composition of lutein, beta-carotene and lycopene in *synergistic amounts* that *decreases age associated DNA damage* in a subject.

Babish teaches a dietary supplementation that scavenges reactive oxygen species. Babish's formulation comprises a single carotenoid species and a second component selected from lipoic acid, dihydrolipoic acid (DHLA), a stilbene species, ergothioneine, a flavone species, a triterpene species, and ascorbic acid. The preferred carotenoid species is astaxanthin for its antioxidant synergy with the selected second components. (See paragraphs [0067]-[0095] of Babish's specification.) However, Babish provides no evidence or support that other carotenoids can act synergistically with the second components, or that lutein, in particular, can act synergistically with beta-carotene and lycopene.

Babish as evidenced by Hoshino does not teach or suggest any composition in amounts sufficient to decrease DNA damage. Moreover, Babish has no appreciation that in a composition comprising *about 0.1 to 20 mg lutein*, beta-carotene and lycopene can act *synergistically* to *decrease DNA damage* in the subject as recited in claims 1, 6, 8 and 16. In fact, none of the examples of Babish measure DNA damage, let alone demonstrate a decrease in DNA damage.

Since Babish fails to teach the claimed compositions and methods, Babish necessarily fails to anticipate claims 1, 6, 8 and 16 and dependent claims 2, 5-7, 10, 13, 15 and 18. Therefore, claims 1-3, 5-10, 13 and 15-18 are novel and patentable in light of Babish. Applicants respectfully request reconsideration and withdrawal of the anticipation rejection.

Nonobviousness of the Pending Claims

Claims 1-20 stand rejected under 35 U.S.C. 103(b) as being unpatentable over Babish et al. (US Pub. No. 2002/0110604 A1) in view of Auweter et al. (US Pub. No. 2002/0044991). The Office Action states that Babish teaches a formulation that contains a carotenoid species selected from astaxanthin, beta-carotene, lutein, and lycopene. The Office Action cites Auweter as teaching at least two active compounds in a multicore structure. The Office Action states that "[o]ne skilled in the art would have been motivated to employ the teachings of the mentioned above references since they relate to a composition comprising of carotenoid species in a nutritional and pharmaceutical formulation." Applicants respectfully disagree.

The rejection fails because the combination of Babish and Auweter does not teach or suggest the claimed invention and there is no reason to modify the prior art.

Babish and Auweter Do Not Teach or Suggest Claimed Invention

Babish teaches a formulation with a single carotenoid species selected from astaxanthin, beta-carotene, lutein, and lycopene (paragraph [0058] of Babish). Babish's formulations all include astaxanthin with a selected second component to demonstrate radical scavenging activity. However, Babish only teaches a single carotenoid species in each formulation, which the Office Action acknowledges. The Office Action then attempts to remedy the deficiencies of Babish by citing Auweter as teaching a multicore structure with one or more carotenoids. However, the combination still fails to teach or suggest the claimed invention of a composition or method of administering a composition comprising *about 0.1 to 20 mg lutein*, together with beta-carotene and lycopene that act *synergistically* to *decrease DNA damage*.

Neither Babish or Auweter teach or suggest any formulation that *decreases age associated DNA damage* as in claims 1 and 16 or *decreases oxidative DNA damage* as in claim 8. In fact, Babish only suggests that astaxanthin demonstrates *scavenging of reactive oxygen species* when combined with a second adjuvant component, such as lipoic acid, dihydrolipoic acid (DHLA), a stilbene species, ergothioneine, a flavone species, a triterpene species and ascorbic acid. Thus, Babish actually teaches away from the present invention by emphasizing the need for non-carotenoid adjuvants. Babish makes no mention of *decreasing DNA damage* or

even appreciates that combining *about 0.1 to 20 mg lutein* and sufficient amounts of beta-carotene and lycopene can act *synergistically* to *decrease DNA damage*.

The additional teachings of Auweter also do not suggest any role of lutein, beta-carotene and lycopene alone or in the recited amounts to decrease DNA damage. Thus Babish in view of Auweter does not teach or suggest the invention of claims 1-20.

No Reason to Modify Babish and Auweter

Moreover, any modifications to the references cannot be obvious without providing some motivation to do so. *See In re Gordon*, 733 F.2d 900, 902, 221 U.S.P.Q. (BNA) 1125, 1127 (Fed. Cir. 1984) ("The mere fact that the prior art could be so modified would not have made the modification obvious unless the prior art suggested the desirability of the modification."); *Northern Telecom, Inc. v. Datapoint Corp.*, 908 F.2d 931, 935, 15 U.S.P.Q.2d (BNA) 1321, 1324 (Fed. Cir. 1990), *cert. denied*, 498 U.S. 920, 112, L. Ed. 2d 250, 111 S. Ct. 296 (1990) ("Whether the changes from the prior art are 'minor,' . . . the changes must be evaluated in terms of the whole invention, including whether the prior art provides any teaching or suggestion to one of ordinary skill in the art to make the changes that would produce the patentee's method and device."). Though Babish seemingly provides a composition with activity against reactive oxygen species, no person having ordinary skill in the art at the time the invention was made would have had any reason or motivation to look to Auweter to modify Babish's formulation to *about 0.1 to 20 mg lutein* and sufficient amounts of beta-carotene and lycopene to act *synergistically* to *decrease DNA damage*.

Auweter provides no teachings or suggestions to synergistic combinations or decreasing DNA damage. Therefore, one of ordinary skill in the art would not be inclined to combine Auweter with Babish to obtain a composition or a method of administering a composition having *about 0.1 to 20 mg lutein* and sufficient amounts of beta-carotene and lycopene to act *synergistically* to *decrease DNA damage*.

Furthermore, one of ordinary skill in the art would not recognize any utility of combining Auweter with Babish since the primary benefits described by Auweter, specifically increased stability of the active ingredients, are not identified as problems by Babish. Babish utilizes a

commercial preparation of astaxanthin and describes no problems with stability, bioavailability or the formation of aggregates -- the benefits taught by Auweter's composition.

Since Babish does not teach or suggest the use of a synergistic combination of lutein with beta-carotene and lycopene in amounts sufficient to synergistically decrease DNA damage, one of ordinary skill in the art would have no reason to look to Auweter. Therefore, no valid reason exists to combine the references other than the Applicants invention and the combination does not render the claimed invention obvious, claims 1-20 are patentable over Babish and Auweter. Applicants respectfully request reconsideration and withdrawal of the obviousness rejection.

CONCLUSIONS

In summary, reconsideration and allowance are respectfully requested for the present application. In the event that the amendments and remarks do not place this case in condition for allowance, an interview with the Examiner and his supervisor is requested prior to the issuance of a final Office Action. The Examiner is invited to call the undersigned at the telephone number below so that a personal or telephonic interview can be scheduled if there are any remaining questions regarding patentability.

Applicant also hereby petitions under 37 CFR 1.136(a) for a two month extension of time or for as many months as are required to ensure that the above-identified application does not become abandoned.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 141449, under Order No. 108341-28.

Dated: March 21, 2011

Respectfully submitted,

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